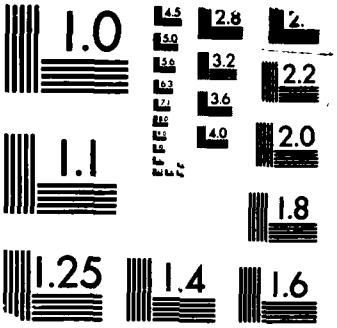
AD-A193 707 INDUCTIONS OF SUPEROXIDE DISMUTASE BY ULTRAVIOLET IRRADIATION AND BY MANG.. (U) DUKE UNIV MEDICAL CENTER DURHAM NC DEPT OF BIOCHEMISTRY I FRIDOVICH 01 FEB 88 1/1

UNCLASSIFIED ARO-21328.51-LS DAAG29-85-K-0013 F/G 7/3 NL



MICROCOPY RESOLUTION TEST CHART

INDUCTIONS OF SUPEROXIDE DISMUTASE BY ULTRAVIOLET IRRADIATION AND BY MANGANESE

Irwin Fridovich

February 2, 1988

U. S. Army Research Office

DAAG29-85-K-0013

Department of Biochemistry
Duke University Medical Center
Durham, North Carolina 27710

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION: Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution unlimited.
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S): ARO 21328.51-LS
6a. NAME OF PERFORMING ORGANIZATION: Department of Biochemistry, Duke University Medical Center; 6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION: U. S. Army Research Office
6c. ADDRESS (City, State, and ZIP Code): Durham, North Carolina 27710	7b. ADDRESS (City, State, and ZIP Code): P. O. Box 12211, Research Triangle Park, NC 27709-2211
8a. NAME OF FUNDING/SPONSORING ORGANIZATION: U. S. Army Research Office; 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER: DAAG29-85-K-0013
8c. ADDRESS (City, State, and ZIP Code): P. O. Box 12211, Research Triangle Park, NC 27709-2211	10. SOURCE OF FUNDING NUMBERS: PROGRAM ELEMENT NO. / PROJECT NO. / TASK NO. / WORK UNIT ACCESSION NO.

11. TITLE (Include Security Classification): Inductions of Superoxide Dismutase by Ultraviolet Irradiation and by Manganese

12. PERSONAL AUTHOR(S): Irwin Fridovich

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Final	FROM 12/1/84 TO 11/30/87	1988 2/1	3

16. SUPPLEMENTARY NOTATION: The view, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other documentation.

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

We have set out to study the inductions of superoxide dismutase and we have done that and a variety of other related projects. We find that the E. coli MnSOD gene is controlled by a repressor protein which can exist in two states i.e. reduced or oxidized. In the reduced state it blocks transcription of the MnSOD gene and in the oxidized state it does not. In soluble extracts of E. coli the repressor can be reduced by glutathione but not by cysteine and by NADPH but not by NADH. The redox-active component of the repressor could be either a transition metal cation such as iron or a disulfide/thiol couple. This cannot yet be decided. The protein coded for by the MnSOD gene is first released in the form of an inactive precursor, distinct from the apoprotein and is then converted to the apoprotein. Final metal insertion to produce the active holoenzyme occurs much more readily under aerobic than under anaerobic conditions. As a consequence the inactive apoprotein, or a form with a metal other than manganese at the active site, accumulates under anaerobic conditions unless the medium is markedly enriched with Mn(II).

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION	
☐ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	Unclassified	
22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE (Include Area Code)	22c. OFFICE SYMBOL

(19) This does not happen in the presence of O_2, presumably because the manganese is then oxidized to Mn(III); which is bound to the active site with greater affinity than is Mn(II). Since O_2^- can oxidize Mn(II) and since we think that iron competes with manganese for the active site of the enzyme, we combined iron-chelating agents, with Mn(II) salts in the presence of aerobic paraquat and achieved striking production of MnSOD by E. coli.

Another series of studies bears upon the biological effects of vanadate. We have found that vanadate catalyzes the oxidation of NAD(P)H by O_2^- and that the mechanism involves a free radical chain reaction. Since this chain reaction amplifies the consequences of the initiating event it has allowed the demonstration that plasma, microsomal and mitochondrial membranes produce and release the superoxide radical.

Perusal of the list of publications which acknowledge support from the AROD office will indicate the full range of our work.

END
DATE
FILMED
7-88
DTIC